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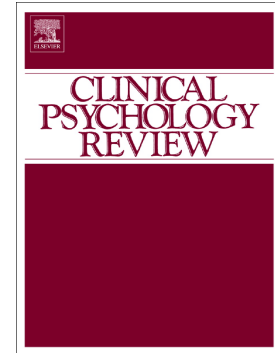
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Dopamine, cognitive biases and assessment of certainty:
A neurocognitive model of delusions

Annabel Broyd^a, Ryan P Balzan^b, Todd S Woodward^c, Paul Allen^{a,d}.

^a Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience (IoPPN), King's College, London, UK

^b School of Psychology, University of Adelaide, SA, Australia

^c Department of Psychiatry, University of British Columbia, Vancouver, BC, Canada

^d Department of Psychology, University of Roehampton, London, UK

Corresponding Author:

Paul Allen Ph.D

Professor of Cognitive Neuroscience

Dept of Psychology, University of Roehampton

Visiting Professor, Institute of Psychiatry, Psychology and Neuroscience, King's College
London, UK

Email: Paul.Allen@roehampton.ac.uk (CC: annabelbroyd@gmail.com)

Tel: 02083925147

Abstract

This paper examines the evidence that delusions can be explained within the framework of a neurocognitive model of how the brain assesses certainty. Here, ‘certainty’ refers to both low-level interpretations of one’s environment and high-level (conscious) appraisals of one’s beliefs and experiences. A model is proposed explaining how the brain systems responsible for assigning certainty might dysfunction, contributing to the cause and maintenance of delusional beliefs. It is suggested that delusions arise through a combination of perturbed striatal dopamine and aberrant salience as well as cognitive biases such as the tendency to jump to conclusions (JTC) and hypersalience of evidence-hypothesis matches. The role of emotion, stress, trauma and sociocultural factors in forming and modifying delusions is also considered. Understanding the mechanisms involved in forming and maintaining delusions has important clinical implications, as interventions that improve cognitive flexibility (e.g. cognitive remediation therapy and mindfulness training) could potentially attenuate neurocognitive processes.

Keywords

Delusions; beliefs; assigning certainty; neurobiological; cognitive; dopamine

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Delusional Beliefs

Delusional beliefs are defined as highly improbable beliefs that are held with strong conviction and are not modified in the face of evidence to the contrary (American Psychiatric Association, 2013). Delusions are cardinal symptoms of psychosis and present in schizophrenia spectrum disorders, mania and psychotic depression, but may also occur in other presentations such as Alzheimer's disease, obsessive compulsive disorder and within the nonclinical population (Cowen, Harrison, & Burns, 2012). While innocuous delusions are relatively common within the 'normal' population (Johns & Van Os, 2001), in clinical populations delusions are associated with lower levels of wellbeing (Broyd, Jolley, & Johns, 2016; Freeman et al., 2014) and are often accompanied by significant distress, depression and anxiety (Smith et al, 2006), particularly if they are persecutory in nature (Freeman, Garety, Kuipers, Fowler & Bebbington, 2002). In such cases, people can become highly preoccupied with their beliefs, and they can impact significantly on their personal, social and occupational functioning (Freeman, 2007).

People with delusions often report highly compelling subjective experiences (Chapman, 1966), even though their beliefs are, by definition, at odds with the environment they have actually encountered (Moritz & Woodward, 2006a). This suggests underlying interference in a range of metacognitive and neurocognitive systems involved in perception, reasoning, belief formation and the appraisal of one's experiences. In this article we will examine the evidence that delusions can be explained within the framework of neurocognitive models of how the brain assesses the certainty of perceptions, beliefs and thoughts. We will consider the empirical evidence for these neurocognitive models and their limitations. Finally, based on the existing evidence base, we propose a model explaining how alterations in the brain systems responsible for assigning certainty contribute to the cause and maintenance of delusional beliefs.

Assigning Certainty

Although 'assigning certainty' can be interpreted as a unitary confidence judgment (Fleming, Dolan, & Frith, 2012; Insabato, Pannunzi, Rolls, & Deco, 2010; Rolls, Grabenhorst, & Deco, 2010), here it will refer to two different but related processes (see White, Engen, Sorensen, Overgaard, & Shergill, 2014). Firstly, it will refer to the ability to assign certainty to objective information provided by a stimulus, event, behaviour or cognitive state. This involves a 'low-level' inference based on the perceived characteristics of a stimulus. Secondly, assigning certainty will refer to the subjective confidence or feelings of conviction associated with a particular belief or experience. This constitutes a

‘high-level’ (conscious) judgment that relies on metacognitive ability (reasoning or beliefs about one’s own cognitions) (Sandberg, Timmermans, Overgaard, & Cleeremans, 2010). Subjective feelings of conviction (or certainty) in one’s beliefs will therefore rely both on the quality of perceptual information received (e.g. consistent stimulus and lack of interfering brain processes) as well as the capacity to self-scrutinise one’s inference.

Bottom-up and Top-down Processing

The ways in which the brain perceives, attends to and processes perceptual information can be considered either a ‘top-down’ or a ‘bottom-up’ process (for review see Theeuwes, 2010). Bottom-up attentional control is stimulus-driven, i.e. attention is spontaneously oriented towards an incoming stimulus. Our *high-level* beliefs can therefore be conceptualised as being influenced by our *low-level* environmental perceptions through bottom-up processing. In contrast, top-down attentional control is intentional and cognitively driven, i.e. directed by knowledge, expectation and current goals (Desimone & Duncan, 1995). Top-down processing can conversely be conceptualised as our pre-existing high-level beliefs and knowledge exerting an influence on low-level perceptions of the environment. In simple terms, bottom-up processing leads us to believe what we perceive and top-down processing leads our perceptions to be biased or altered in line with what we already believe. Importantly, top-down and bottom-up processes represent overlapping organizational principles, and interact to optimize attentional performance (Sarter, Givens, & Bruno, 2001) but are associated with different brain networks (Corbetta & Shulman, 2002).

Perceptions therefore arise from an interaction between ‘top-down’ functions (e.g. learned expectations, hypotheses and reasoning) and objective stimulus data (Delorme, Rousselet, Macé, & Fabre-Thorpe, 2004; Mechelli, Price, Friston, & Ishai, 2004). According to such a model, it is possible for ‘top-down’ goals to influence the perception of one’s environment (Theeuwes, 2010). A classic example of this is the slower and less accurate recognition that arises when an object presented in a particular scene violates the surrounding contextual information or is of an inappropriate size or location (e.g. a fire extinguisher sitting directly on top of a post box in a street scene) (Biederman, Mezzanotte, & Rabinowitz, 1982). This seems to indicate that contextual cueing or ‘priming’ can influence perception in a top-down fashion.

Theoretical Accounts of Delusions

A number of theoretical accounts have been put forward to explain delusions. As they are theoretical frameworks, they do not require evidence of empirical association with the severity of delusions. However, as will be addressed below, some have been tested empirically.

Aberrant Perceptions

It has been suggested that delusional beliefs arise as a secondary response to aberrant or erroneous perceptions (Escher, Romme, Buiks, Delespaul, & van Os, 2002; Krabbendam et al., 2004). For example, Maher (Maher, 2005, 2006) argues that “bizarre” or delusional interpretations are a rational response to anomalous but genuine sensory experiences such as auditory or visual hallucinations that are also common in psychosis (Nayani & David, 1996). This account is consistent with the idea that certainty judgments can be erroneous at a basic low-level perceptual inferences level, which, then alter subjective high-level interpretations (i.e. arising through bottom-up processes). This seems consistent with the experiences of people with highly specific or ‘monothematic’ delusions. One such example is the ‘Capgras delusion’, which involves the highly compelling and specific belief that a friend or family member has been replaced by an imposter (in the absence of psychosis elsewhere) (Ellis, Young, Quayle, & De Pauw, 1997). The Capgras delusion has been explained through disconnection between an intact face recognition system and an intact autonomic nervous system. According to this account, the delusion arises from the patient attempting to explain the anomalous experience of recognising a familiar face in the absence of the usual affective response associated to that face (Coltheart, Langdon, & McKay, 2007; Coltheart, Menzies, & Sutton, 2010; Davies, Breen, Coltheart, & Langdon, 2001). This leads familiar faces to be perceived as strangers through dysfunctional bottom-up processes. However, a purely bottom-up explanation of delusions does not seem to account for delusional beliefs in the absence of perceptual disturbance (e.g. hallucinations), fails to account for the experiential qualities of delusions, and equally fails to explain why some unusual experiences and perceptions do not develop into delusions (Bell, Halligan, & Ellis, 2008; Hohwy, 2004; Langdon & Coltheart, 2000).

An alternative account proposes that pre-existing beliefs and reasoning and attentional biases may exert a ‘top-down’ influence to alter one’s perception of sensory information (Adams, Stephan, Brown, Frith, & Friston, 2013; Fletcher & Frith, 2009). For example, Campbell (2001) disagrees that monothematic delusions arise through bottom-up processes, arguing instead that beliefs such as the Capgras delusion would not occur without a disruption of the top-down loading of one’s fundamental

beliefs influencing one's perceptual experience. For example, feelings of familiarity and memories associated with a particular person may be impaired at higher levels, which could alter perceptions of the person in a top-down fashion (Bayne & Pacherie, 2004). This account would suggest that delusions may arise through high-level certainty judgments influencing sensory experiences in a top-down way, although there is no convincing empirical evidence to support that monothematic delusions arise in this way.

Predictive Coding

An influential account of delusions posits that they arise from a single core abnormality in updating beliefs and inferences in a Bayesian (or probabilistic) fashion (Adams et al., 2013; Fletcher & Frith, 2009; Hohwy, 2013). This account rests on the premise that the biological (neural), cognitive and experiential features of delusions are all explained through a unitary abnormality in predictive coding. Predictive coding refers to a brain process that aims to maximise cognitive efficiency by using prior experience to predict incoming sensory information. 'Surprise' (or 'prediction error') may occur when a person's learned expectations conflict with objective sensory input. Cognitive resources are then preferentially allocated to processing this novel information (Fletcher & Frith, 2009). This means that novel experiences that are consistent with pre-existing beliefs may be ignored or receive less attention due to their predictability, while those that are inconsistent with beliefs (and therefore 'surprising' or interesting) may be preferentially attended to and/or acted upon.

In delusions, 'false' prediction error signals may arise at lower levels in the brain and, through cognitive attempts to reduce the prediction-error signal (which indicates that pre-existing beliefs are not adequately accounting for the perceived input), adjustments will then be made at higher cognitive levels in order to minimise this discrepancy. Therefore false prediction error signals are thought to 'propagate up a belief hierarchy' (a 'Bayesian hierarchy') to form delusions. Within a framework of assigning certainty, the predictive coding account can be conceptualised as an inability to assign certainty at the low/perceptual level, which through bottom-up propagation can influence high-level certainty/beliefs. By definition, delusions are fixed false beliefs, so involve an impaired ability to update beliefs and inferences, that can be modelled by a Bayesian (or probabilistic) approach or other statistical approaches to modelling change or lack thereof. However, it is valuable to build the foundation of a theoretical account of delusions on evidence of existing emotional and cognitive biases that additionally address the phenomenological aspects of delusions, such as why the content of delusions are often personally, environmentally and culturally relevant (Suhail & Cochrane, 2002), and that have been empirically validated as associated with the severity of delusions.

The Two-Factor Theory

Another account posits that two factors are necessary for the development and maintenance of delusions. The first factor accounts for the *content* of a delusion, and may include the perceptual aberrations discussed above, which can lead to the development of delusional hypotheses through a bottom-up process. Due to the varied content of delusions, it is assumed that this first factor varies from delusion to delusion, and it is this first factor that initially prompts the delusional belief (Coltheart, Langdon & McKay, 2007). The second factor accounts for why this delusional hypothesis, once formulated, is *adopted* and *maintained* despite the availability of potentially overwhelming counter-evidence (Coltheart et al., 2007; Coltheart, Langdon, & McKay, 2011; Davies, Coltheart, Langdon, & Breen, 2001; Langdon & Coltheart, 2000; McKay, Langdon, & Coltheart, 2005a). The nature of this second factor has been modified gradually over time; early attempts to conceptualise it maintained that it was an “all-or-none” deficit present in delusional people but absent in healthy individuals (Langdon & Coltheart, 2000). It is now considered to be a neurocognitive impairment at the extreme end of a belief evaluation continuum (McKay, Langdon, & Coltheart, 2005b). This impairment in belief evaluation is thought to explain why delusional beliefs are adopted and why they persist, and are so resistant to rational counter-argument (Coltheart et al., 2011). Moreover, unlike the first factor which varies according to delusional content, it is assumed that this second factor remains constant and will be present regardless of the specific delusional theme (Coltheart et al., 2011). There is also preliminary neurological evidence to suggest that this second factor is associated with damage to the right lateral prefrontal cortex (Coltheart et al., 2007). The rationale for incorporating the second factor arose from evidence from neuropsychological patients with damage to brain areas that influence their perceptual systems, but who do not exhibit the delusions that one might expect if delusions were exclusively generated through a bottom-up process (whereby the belief is generated through rationalising aberrant low-level perceptions). For example, Tranel et al. (1995) reported how patients with damage to their orbitofrontal cortex showed impaired autonomic nervous system responses to familiar faces, but did not develop the Capgras delusion. This suggests that high-level factors must be implicated *in addition* to low-level perceptual processes. Therefore this account posits that delusions are formed through disruption to a combination of both low and high-level certainty judgments, but unlike the unitary predictive coding model, the first low-level factor is a necessary precursor for delusions to arise. While the two-factor theory is helpful in conceptualising specific monothematic delusions in neuropsychological patients, the high-level belief evaluation component or ‘second factor’ seems insufficient in explaining delusions in psychosis, which often reflect personal experiences of trauma and persecution (Reiff, Castille, Muenzenmaier, & Link, 2012; Thompson et al., 2010) as well as an individual’s social and cultural context (Cannon & Kramer, 2012; Catone, Pisano, Broome,

Lindau, Pascotto, & Gritti, 2016). This would suggest that a model that acknowledges the involvement of pre-existing beliefs and experiences might provide a more parsimonious explanation of delusions.

Interactionist Account of Delusions

Young (2008) attempted to consolidate previous theories by explaining the aforementioned ‘Capgras delusion’ in the context of a bi-directional interaction between bottom-up and top-down processes. By this account, cognitive deficits and phenomenological aspects of the Capgras delusion actually cause the person’s experience of their friend or family member to be *restructured* so that they align with their beliefs. In other words, the experiential qualities of the delusion serve to validate the belief held regarding the friend or family member (in a bottom-up fashion) but the belief also reciprocally provides authenticity to the experiential qualities in a top-down way. The interactionist account clearly fits with the idea that delusions may arise from aberrance in assigning certainty at both high and low-levels in the brain, and through reciprocal interactions between top-down and bottom-up processes. While the model should be commended for incorporating delusional phenomenology, it has only been applied to explain this rare and specific delusion, lacks an empirical evidence base, and therefore may differ across disorders or other types of delusion.

Neuroscientific Accounts of Delusions

Neuroscientific accounts of delusions involve putting forward a biological mechanism combined with a cognitive concept, with the degree of empirical association with the severity of delusions not required but sometimes collected.

Dopamine and Aberrant Salience

Although no clear neurocognitive model of certainty judgements exists, a number of neurobiological systems are thought to be involved in this process and dysregulation of these systems may lead to the development of delusion beliefs. Elevated dopamine synthesis is widely reported in individuals with psychosis (Dao-Castellana et al., 1997; Laruelle, Abi-Dargham, Gil, Kegeles, & Innis, 1999; Lindstrom et al., 1999; Reith et al., 1994). Indeed, Howes et al. (2011) found that striatal dopamine increases progressively as psychosis develops. Although this does not necessarily imply a causal relationship between dopamine and psychosis, meta-analyses have revealed strong evidence for

elevated dopamine synthesis capacity in schizophrenia (Fusar-Poli & Meyer-Lindenberg, 2012; Howes, Kambeitz, Kim, & et al., 2012). Furthermore, as antipsychotic medication is often effective in attenuating psychotic symptoms (Howes & Kapur, 2009) and amphetamines are able to induce psychosis in healthy volunteers (Angrist & Gershon, 1970; Yui, Ikemoto, Ishiguro, & Goto, 2000) (both of which act on dopamine receptors in the striatum), this suggests that altered dopaminergic neurotransmission may underlie psychosis specifically.

Dopamine neurons are implicated in processing rewarding (Schultz, 2002; Wise, 2004) and novel (Ljungberg, Apicella, & Schultz, 1992) stimuli, including objects, behaviours or internal states (Winton-Brown, Fusar-Poli, Ungless, & Howes, 2014). The ‘aberrant salience hypothesis’ (Kapur, 2003, 2004; Kapur, Mizrahi, & Li, 2005) proposes that a hyperactive dopamine system in the midbrain and striatum (Davis, Kahn, Ko, & Davidson, 1991; Seeman & Kapur, 2000) leads to contextually irrelevant salience attribution in response to otherwise non-salient stimuli and internal representations. Specifically, people diagnosed with schizophrenia seem to assign excessive salience to contextually-irrelevant events, but show dampened salience attribution in response to conventionally salient stimuli (Kapur et al., 2005; Murray et al., 2008; Roiser et al., 2009). As such, perturbed striatal dopamine function may disrupt the ability to revise or update beliefs in a ‘Bayesian’ (Fienberg, 2006; Mathys, Daunizeau, Friston, & Stephan, 2011) or probabilistic fashion (Fletcher & Frith, 2009; Hemsley & Garety, 1986). This refers to the inferential process of updating beliefs through integrating new evidence with pre-existing knowledge or schemas about the world. The aberrant salience hypothesis can equally be explained by delusions arising through disruption to a person’s ability to assign high-level certainty to one’s experiences in a top-down fashion. Tasks assessing salience tend to compare patients with psychosis or schizophrenia to healthy controls (e.g. Jensen et al., 2008; Murray et al., 2008) rather than assessing the specific association between salience and delusion severity. Notably, Roiser et al. (2013) reported a positive correlation between the degree of aberrant salience and delusion-like symptoms in a sample of people at high risk of developing psychosis. This provides evidence for a link between aberrant salience and delusions specifically, that is not confounded by the effects of illness and medication (e.g. Abboud et al., 2016).

Dopamine and Prediction Error

Prediction-error arises when there is a mismatch between what a person expects (based on a learned probabilistic estimation from prior evidence) and the actual sensory input (Rescorla & Wagner, 1972). In the brain, such a discrepancy or ‘surprise’ is expressed through the dopaminergic-dependent prediction-error signal in the striatum when the surprise is related to rewarding stimuli (Hollerman &

Schultz, 1998). However, there is some evidence to suggest that mesolimbic, mesocortical and nigrostriatal dopamine neurons also respond to the presentation of non-rewarding novel stimuli (Horvitz, 2000). To reconcile these neurobiological observations with neurocognitive models, it could be argued that the dopamine mediated prediction error is generated when there is a mismatch between bottom-up perceptual evidence/low-level certainty and top-down pre-existing beliefs/high-level certainty (Fletcher & Frith, 2009). Accordingly, functional magnetic resonance imaging (fMRI) studies have identified abnormal striatal prediction-error signals on associative learning tasks in people with psychosis (Jensen et al., 2008), even when they are medication naïve (Murray et al., 2008; Schlagenhauf et al., 2014). For example, whilst controls show robust activation in the dopaminergic midbrain and ventral tegmental area/substantia nigra (containing dopaminergic cell bodies projecting to the striatum) in response to rewarding stimuli, medication-naïve patients actually exhibit greater activation in response to neutral stimuli and reduced activation patterns in response to rewarding stimuli (Murray et al., 2008). Furthermore, the extent of prediction-error disruption in people diagnosed with schizophrenia also seems to be significantly associated with the tendency to form delusions (Corlett et al., 2007; Gradin et al., 2011). Delusions may act as an explanation for the ‘sensory overload’ and confusion that occurs when novel and salient stimuli conflict with existing mental representations and beliefs over long time periods (Winton-Brown et al., 2014). Therefore, within a framework of assigning certainty and according to the Dopamine and Prediction Error account, delusions arise from the mind rationalising these abnormal perceptual experiences, aberrantly assigning certainty via a stimulus-driven bottom-up route. Perturbed striatal dopamine function, prediction errors and aberrant salience may also affect hippocampally mediated episodic memory formation and long term potentiation (Lisman & Grace, 2005), a process thought to be crucial during the development of psychosis (Modinos, Allen, Grace, & McGuire, 2015). It is possible that impaired episodic memory formation impacts on belief formation and systems that ultimately feed and maintain delusions.

Salience Network

Neuroimaging studies have also revealed disruption to the neural substrate thought to orient attention to salient stimuli in people with schizophrenia (regardless of delusional symptom profile) compared with controls; namely the ‘frontal salience network’, comprising the bilateral insula and dorsal anterior cingulate cortex (Menon, 2011; Seeley et al., 2007; White, Joseph, Francis, & Liddle, 2010). There seems to be converging evidence indicating that the salience network is activated by orienting stimuli. A detailed review by Menon (2011) highlights how the salience network is consistently coactive with task-specific regions when stimuli are modulated in terms of cognitive,

emotional and homeostatic salience, suggesting they fundamentally code salience. Furthermore a meta-analysis by White et al. (2014) demonstrated that the brain regions most consistently activated in times of environmental uncertainty were the salience and central executive network. Studies also show that the salience network is important for response inhibition (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; Aron, Robbins, & Poldrack, 2004), suggesting that the salience network is activated early and the signal it generates codes whether or not an individual should respond. There is robust evidence of grey matter volumetric reductions in the anterior cingulate and anterior insula in patients with schizophrenia relative to controls (Baiano et al., 2007; Honea, Crow, Passingham, & Mackay, 2005; Palaniyappan, Mallikarjun, Joseph, White, & Liddle, 2011). Furthermore, volume alterations in these areas are significantly correlated with severity of delusions (Palaniyappan et al., 2011). Functional MRI has also identified dysregulation of the salience network in schizophrenia on a reward-related learning task (White, Gilleen, & Shergill, 2013). This paper also found that in healthy controls, but not people with schizophrenia, the salience network was more active when stimuli carried more incentive salience than at times when they carried less incentive salience. Roiser and colleagues (2013) also found that both aberrant salience and ventral striatal responses were related to delusion severity in people at ultra high risk of psychosis. These studies further suggest that delusions may involve both structural and functional disruption to the salience network. The meta-analysis by White et al. (2014) has also corroborated that the salience network responds specifically to low-level environmental uncertainty in healthy volunteers, assessed through tasks that modulate predictability of environmental stimuli (e.g. rewards-based, gambling, probability based tasks). It is conceivable that disruption to the salience network might interfere with low-level perceptual/certainty judgments, giving rise to delusions through bottom-up processing (consistent with the ‘aberrant perceptions’ theoretical account of delusions).

Other Neurobiological Processes

Neuroimaging studies in people with schizophrenia have revealed altered function, volume and connectivity in a range of brain regions, including the prefrontal cortex (Barch, Carter, Braver, & et al., 2001; Weinberger, Berman, & Zec, 1986), the medial temporal lobe (Wright et al., 2000), the anterior cingulate cortex (Kerns et al., 2005), language regions (Woodward, Tipper, Leung, Lavigne, Sanford, & Metzak, 2015; Lavigne et al., 2015) and ‘default mode network’ (a network spanning the ventral medial prefrontal cortex, the dorsal medial prefrontal cortex, the posterior cingulate cortex, precuneus and the lateral parietal cortex) (Garritty et al., 2007; Woodward et al., 2016; Lavigne et al., 2015). It is not clear at present how striatal dopamine dysregulation might contribute to functional alterations in these other regions. However, it seems there are multiple systems and networks involved in delusion

formation and maintenance (although there may well be a single unitary developmental pathology upstream giving rise to these alterations). It is therefore also important not to discount the role of other neurotransmitters, which may contribute to delusions through interactions in complex neurocircuits. For example, hyperactivity in the hippocampus due to dysregulation of glutamatergic and GABAergic systems, leads to increased ‘downstream’ dopamine in the striatum and midbrain (Lodge & Grace, 2011), possibly disrupting the detection of novel/salient stimuli (Modinos et al., 2015). Acetylcholine (Martin & Freedman, 2007) and noradrenaline (Yamamoto & Hornykiewicz, 2004) also seem to be implicated in psychosis and warrant further empirical attention in relation to delusions. Furthermore, atypical antipsychotics, which are effective in attenuating psychotic symptoms, are thought to work on a number of other neurotransmitter systems (e.g. Van der Heijden et al., 2004) in addition to D2 receptor blockade (Keshavan, Lawler, Nasrallah, & Tandon, 2016; Miyamoto, Miyake, Jarskog, Fleischhacker, & Lieberman, 2012). This suggests that other mechanisms, such as the serotonergic system, may be implicated in delusions through interfering with high and/or low-level certainty judgments.

Cognitive Accounts of Delusions

Cognitive models or approaches to delusions usually rely upon behavioural tasks or measures to establish an empirical association between a purportedly aberrant behaviour or cognitive process and the severity of delusions. Some studies report a difference between delusional and non-delusional patients (e.g. Moritz & Woodward, 2005), some report no difference (e.g. Colbert, Peters, & Garety, 2010), and some do not report whether or not there is a difference and base conclusion on the difference between patients with psychosis and healthy controls (e.g. So et al., 2012). Clearly the strongest evidence for the validity of a cognitive test in measuring a cognitive process underlying delusions lies in this empirical association.

Jumping to Conclusions

In order to comprehensively explain how certainty judgments might break down to cause delusions, a satisfactory theory ought to bridge the gap between neuronal and cognitive processes. Bayesian inferencing can be explored behaviourally using probabilistic reasoning tasks such as the ‘bead task’ (Huq, Garety, & Hemsley, 1988). Here, participants are typically presented with two jars containing complementary ratios of coloured beads. The jars are then hidden from view and beads are drawn one at a time from one jar. After each draw, participants are required to estimate which jar the bead has been drawn from and the task is terminated when they have arrived at a final decision. The key prediction is that individuals with delusions express a bias towards estimating from which jar the

beads have been taken with greater certainty and/or more rapidly (e.g. fewer ‘draws to decision’) than healthy control subjects. This tendency to make hasty decisions based on little evidence has been termed the ‘jumping to conclusions’ (JTC) bias (Garety & Freeman, 2013) and reflects an abnormality in assigning appropriate metacognitive confidence to events (a high-level cognitive process).

The JTC bias is the most replicated bias correlated with delusions in the literature to date, and has generated four recently published meta-analyses. The Dudley, Taylor, Wickham, and Hutton (2015) meta-analysis, which included previously unpublished data from 16 authors, confirmed the association between JTC bias on the beads task and clinical delusions. A trend-level inverse relationship between data gathering and delusion severity was identified and the JTC bias was also associated with increased probability of delusion occurrence in psychosis. People with psychosis were also found to request less evidence to make decisions and were significantly more likely to display ‘extreme responding’ compared with both healthy individuals and people with non-psychotic mental health problems. The meta-analysis by So, Siu, Wong, Chan, and Garety (2016) concluded that JTC is not a transdiagnostic phenomenon beyond psychosis. Similarly, McLean, Mattiske, and Balzan (2016) found that the JTC bias is associated specifically with delusions rather than with a diagnosis of schizophrenia or another psychiatric disorder, consistent with the possibility that it contributes to delusional severity. Finally, a meta-analysis looking at data-gathering biases on the beads task within the general population found a small significant JTC effect within healthy but ‘delusion-prone’ samples, which minimises the confounding effects of psychosis (e.g., working memory deficits) and medication (Ross, McKay, Coltheart, & Langdon, 2015). Collectively, this meta-analytic data suggests that hasty decision-making is a genuine core abnormality in delusional/delusion-prone individuals and adds to the evidence that aberrant assignment of high-level certainty to one’s beliefs or hypotheses can contribute to delusions in a top-down fashion.

Despite the apparent consistency across the JTC literature, it is also worth noting that several individual studies did not yield significant differences between delusional and non-delusional groups on measures of JTC. This has led some researchers to conclude that there may be challenges associated with accurately measuring JTC with the ‘beads task’. For example, Balzan, Delfabbro, Galletly, and Woodward (2012a) showed that miscomprehension is a potential confound of the bead task, whereby people may incorrectly assume that the purpose of the task is to determine where the current bead is coming from rather than the bead sequence.

Hypersalience of Evidence-Hypothesis Matches

An alternative approach which aimed to address the potential methodological issues of the beads task required participants to provide probability estimates that a fisherman was fishing from two different lakes; Lake A or Lake B (Speechley, Whitman, & Woodward, 2010). Separate rating scales are presented for each lake, as opposed to using one scale (e.g. Lake A at one end and Lake B at the other end of the scale), as is often used in other JTC paradigms. The conventional single scale forces probability estimates for each lake to be reciprocal, for example, if a fish is rated as 30% likely to come from Lake A, the participant must automatically choose that it is 70% likely to come from Lake B, resulting in loss of information regarding a person's reasoning skills. Two scales allow separate measures of lakes, one matching the caught fish (e.g. black fish caught and mostly black fish in the lake) and one not matching the caught fish, (e.g. black fish caught and mostly white fish in the lake). Participants with active delusions rated 'matching lakes' significantly higher earlier in the sequence than all non-delusion groups; however, there were no differences between delusional and non-delusional groups for 'non-matching lakes'. This suggests that the core cognitive operation underlying the JTC bias may be a 'hypersalience of 'evidence-hypothesis' (EVH) matches; that is, data-gathering might cease to occur because the first evidence-hypothesis matches are deemed to be sufficient to make a definite decision. A series of experiments have further validated this mechanism across a number of other cognitive biases, whereby people with delusions were consistently shown to overvalue and attach excessive weight to 'EVH (evidence-hypothesis) matches' whilst considering non-matches normally (Balzan, Delfabbro, Galletly, & Woodward, 2012b; Balzan, Delfabbro, Galletly, & Woodward, 2013; Balzan, Delfabbro, Galletly, & Woodward, 2013).

Liberal Acceptance

It is possible that JTC may also be mediated by other processes. For example, studies have shown that the JTC bias occurs only in situations of relatively low ambiguity (Moritz et al., 2016; Moritz & Woodward, 2004; Moritz, Woodward, Jelinek, & Klinge, 2008; Moritz, Woodward, & Lambert, 2007). For example, while patients diagnosed with schizophrenia show a JTC bias when presented with two jars, the effect seems to disappear when they are presented with four jars (Moritz et al., 2007). This 'liberal acceptance' (LA) account posits that multiple alternatives with similar ratios (higher ambiguity) abolishes the JTC effect in psychosis (Moritz & Woodward, 2004). This would reflect a lower threshold for making decisions, which may be surpassed in the face of relatively limited evidence in favour of one particular option. It therefore seems that in psychosis, subjective feelings of confidence can be inappropriately high even when presented with tentative and unreliable environmental evidence.

Maintenance Factors

Much of the literature fails to account for why delusional beliefs continue to be maintained with such confidence and inflexibility, despite unequivocal environmental evidence to the contrary. Freeman, Garety, Kuipers, Fowler, and Bebbington (2002) argue that persecutory delusions may become ingrained through selectively focusing on evidence that appears consistent with the belief, also known as ‘confirmation bias’. This may involve low-level biases in memory, cognition and attention (e.g. potential hyperactivation in the salience network), which orient the individual towards threatening or belief confirming information (for review see Bentall, Kinderman, & Kaney, 1994). For example, on evidence-hypothesis matching tasks, people diagnosed with schizophrenia, as well as non-clinical delusion-prone participants, show greater bias in their search for confirming evidence, rate confirming evidence as more important than disconfirming evidence and remember the confirming evidence more readily than disconfirming evidence compared with non-clinical controls (Balzan et al., 2013a). Additionally, it has been demonstrated that people with severe delusions are less willing to integrate evidence that disconfirms their interpretations, and it has been proposed that delusions may be maintained through this ‘bias against disconfirmatory evidence’ (BADE), whereby evidence *against* the belief is not fully integrated. People with delusions have demonstrated being less able to adjust their beliefs to be more tenable when providing interpretations of neutral scenarios compared with healthy volunteers and psychiatric controls (Woodward, Buchy, Moritz, & Liotti, 2007; Woodward, Moritz, & Chen, 2006; Woodward, Moritz, Cuttler, & Whitman, 2006; Woodward, Moritz, Menon, & Klinge, 2008). Furthermore, a recent meta-analysis by McLean et al., 2016 has demonstrated that BADE is associated with severity of delusions. A hypersalience of evidence-hypothesis matches may contribute to this impaired integration of new disambiguating information, as previously strengthened evidence-hypothesis matches may be more resistant to change or re-evaluation, whilst disconfirmatory evidence, which does not match initial assumptions, is given substantially less emphasis. This effect for patients with delusions may also be exacerbated with self-generated beliefs (Whitman et al., 2013). This may explain how aberrant ability to assign subjective high-level certainty to one’s beliefs can serve to maintain and strengthen them.

Interestingly, Joyce, Averbeck, Frith, and Shergill (2013) found that patients diagnosed with schizophrenia actually apply similar weight to *new* evidence as healthy controls, but rather tend to ‘leak’ previous (or older) evidence. On a computerised probabilistic reasoning game, patients struggled to detect regularities in their opponent’s play, even when the pattern was obvious. Nevertheless, they still expressed overconfidence in their responses, which were skewed towards favouring newer

evidence with more immediate rewards. Based on their findings, Joyce et al. (2013) posit that delusions may arise through a breakdown in metacognitive ability to assign certainty (JTC bias and overweighting of recent evidence) and are maintained due to inability to integrate temporal information appropriately, which may be due to metamemory deficits in schizophrenia (Moritz & Woodward, 2006b). However, this finding seems to contradict the aforementioned evidence that people with delusions *fail* to integrate novel disambiguating evidence rather than over-incorporating it. If newer evidence were consistently favoured in psychosis, one might expect delusional beliefs to be transiently extinguished when objective environmental evidence conflicts with erroneous pre-existing beliefs. The fixed and chronic nature of delusions suggests that this is not the case (Tandon et al., 2009). As previously mentioned, people with delusions seem to express a hypersalience towards new (hypothesis matching) evidence (leading to the JTC bias). Perhaps evidence-hypothesis matches encountered on the first piece of evidence persist because this initial information remains displayed throughout the remainder of the trial. This provides a potential explanation for the BADE effect and implies that for people with delusions, under everyday, complex decision-making conditions, initial hypothesis-matching evidence may over-ride novel hypothesis-nonmatching evidence. This would suggest that high-level certainty judgments can exert a top-down influence on perceptual or low-level environmental evidence, consistent with the ‘Predictive Coding’ or ‘Interactionist’ theoretical accounts of delusions. Further work is needed to clarify this set of results.

Other Cognitive Biases

It is possible that other cognitive biases influence the ability to self-scrutinise one’s belief (Salvatore et al., 2012). For example, delusional beliefs could arise from overconfidence in errors (Balzan, 2016; Moritz, Woodward, Whitman, & Cuttler, 2005) when making subjective judgments regarding mental states (Kother et al., 2012). Other cognitive biases that may influence high-level confidence estimations include intolerance of ambiguity (McKay, Langdon, & Coltheart, 2006), a bias favouring self-selected hypotheses (Whitman, Menon, Kuo, & Woodward, 2013) and dichotomous or ‘all or nothing’ thinking styles (Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001). Certain types of neurocognitive processes may be related to different types of delusions. For example, biases such as JTC may be related to a top-down phenomenology (e.g. complex or affective delusions), whilst altered dopamine in the absence of higher-level biases may be related to a bottom-up phenomenology such as passivity phenomena.

Dopamine and Cognitive Biases

There is conflicting evidence as to whether dopamine plays a role in influencing higher level certainty judgments, such as JTC. A study by Lou et al. (2011) explored whether increased dopamine neurotransmission in healthy individuals would mediate subjective confidence on a visual perception task. Participants were randomly assigned to receive either Pergolide (a dopamine agonist) or placebo prior to the task. Increased dopaminergic transmission was associated with significantly higher confidence ratings than placebo, suggesting that elevated dopamine may be implicated in over-assigning subjective (high-level) certainty to events. This finding is paralleled by a study by Andreou, Moritz, Veith, Veckenstedt, and Naber (2013) which found that the number of high confidence incorrect responses *reduced* when healthy participants were given haloperidol; a dopamine antagonist, which reduces dopamine transmission by blocking post synaptic D2 receptors. However, the same study found that neither increases nor reductions in dopamine transmission had any effect on the JTC bias. Another study by Ermakova, Ramachandra, Corlett, Fletcher, and Murray (2014) similarly reported no effect on the draws to decision aspect of the JTC bias under administration of another dopamine agonist, methamphetamine. However, Menon and colleagues (2008) found that patients who initiated their antipsychotic medication subsequently demonstrated less hasty decision-making and decreased intensity of delusions. Mizrahi et al. (2006) found that dopaminergic antipsychotic treatment has little effect on delusional *conviction* in people with psychosis, but rather works by dampening symptoms through detaching people from their experiences. These mixed findings suggest there is insufficient evidence at present to confirm that higher-level processes are directly affected by aberrant dopamine. However, it remains plausible that dopamine could influence higher-level explanations and certainty judgments through altering perceptual/low-level experiences in delusions via a bottom-up process, which could be tested empirically.

Emotion, Stress, Trauma and Sociocultural Factors

Emotion seems to be intrinsically linked to delusions (Freeman et al., 2002; Garety & Freeman, 2013) and may influence the way in which certainty is assigned to one's perceptions and thoughts. Persecutory delusions by their very nature involve themes of negative affect (Freeman et al., 2013; Freeman, Garety, & Kuipers, 2001) and depression and low self-esteem are associated with severity of persecutory delusions (Kesting & Lincoln, 2013; Smith et al., 2006). Delusions of grandiosity, on the other hand, are associated with higher self-esteem, lower depression and lower anxiety (Garety et al., 2013; Smith et al., 2006). It therefore seems that delusions are a direct manifestation of an individual's underlying emotional concerns (Freeman & Garety, 2003). Interestingly, state anxiety increases both

paranoid ideation and the JTC bias in healthy participants (Lincoln, Lange, Burau, Exner, & Moritz, 2010), suggesting that transient emotional states may be sufficiently powerful to influence high-level subjective decisions. It seems likely that emotion may influence bottom-up processing through interacting with other cognitive processes such as attentional control to influence severity, content and appraisal of delusional beliefs.

Trauma, drug use and socioeconomic status are related to delusional ideation in the general population (Saha, Scott, Varghese, & McGrath, 2012; Saha, Scott, Varghese, & McGrath, 2013; Saha et al., 2011) and there is very strong evidence for a link between trauma and psychosis (Read, Morrison & Ross, 2005). It is therefore possible that social, cultural and environmental factors interact with neurocognitive processes involved in assigning certainty, to elicit, exacerbate or determine the theme of delusional beliefs. Delusions in psychosis are often persecutory in nature, and evidence suggests there are parallels between past experiences (e.g. trauma) and delusional themes (Reiff, Castille, Muenzenmaier, & Link, 2012; Thompson et al., 2010). Furthermore, the content of delusions tends to change across time periods and according to cultural and societal norms (Cannon & Kramer, 2012; Catone, Pisano, Broome, Lindau, Pascotto, & Gritti, 2016), suggesting that life experiences and pre-existing beliefs are implicated in delusions. Furthermore, stress can directly contribute to exaggerated dopamine release in psychosis (Mizrahi et al., 2012), which could therefore contribute to delusions through influencing low-level certainty judgments. Acute psychosocial stress and drugs of abuse have also been found to increase strength at excitatory synapses on dopamine neurons in the mid-brain of mice (Saal, Dong, Bonci, & Malenka, 2003). Moreover many drugs of addiction specifically work by increasing dopamine action in the brain (Wise & Hoffman, 1992). This draws parallels with the hyper-responsive dopaminergic system in psychosis, which is also reported to occur in brain areas such as the striatum (Kapur, 2003). It seems therefore that external and environmental factors may be able to influence the dopaminergic system as well as high-level certainty judgments, giving rise to psychosis and in particular, delusional beliefs, through both bottom-up and top-down processes.

A Model for Delusion Formation and Maintenance

We propose an integrative model whereby delusions arise through reciprocal top-down and bottom-up interactions between disrupted low and high-level certainty judgments. The model emphasises empirically tested factors and integrates the existing evidence base to conceptualise how delusions might be formed and maintained.

Insert Figure 1 here

Figure 1: Summary model of the formation and maintenance of delusional beliefs.

Firstly, a perturbed dopaminergic system assigns abnormal salience (a low-level certainty judgment) to perceptual information (Kapur, 2003). This process may be supported and reinforced by hyperactivation in ‘bottom-up’ attentional systems (i.e. salience network) and may orient attention towards particularly threatening or anxiety-provoking environmental stimuli. This comes from evidence suggesting salience network alterations in the brains of people with delusions. External factors such as stress, state anxiety and drugs may influence the dopamine system and thereby increase propensity to assign inappropriate salience to experiences (Saal et al., 2003). Cognitive factors including JTC bias (mediated via a mechanism of liberal acceptance and hypersalience of evidence-hypothesis matching) also interfere with the ability to assign confidence to experienced perceptual events in a top-down fashion. For example, reduced top-down influence on sensory input which prevents new information from being appropriately integrated with existing knowledge could be modelled by Bayesian mathematics (Corlett et al., 2007).

Emotion, personal experiences (e.g. trauma) and sociocultural factors interact with these neurocognitive processes to determine the theme, severity and appraisal of the delusional belief (Freeman & Garety, 2003), which may occur at a low/perceptual (Phelps, Ling, & Carrasco, 2006) or high/conscious (Lerner & Keltner, 2000) level. These factors may also interact to determine the levels of distress and paranoia associated with the delusional belief. Once formed, delusions may fail to be extinguished as environmental stimuli continue to be experienced in an aberrant fashion (due to a perturbed dopamine system). Cognitive vulnerabilities including poor metamemory (Moritz & Woodward, 2006b), confirmation bias and BADE may prevent invalidation of delusional beliefs.

Recommendations for Future Research

Our model may become further refined and updated as more empirical evidence is gathered. Future research should aim to explore low-level certainty and high-level confidence as two different, but reciprocally related processes in order to further establish the neurocognitive processes involved in delusions. Research should also progress further beyond the role of dopamine to investigate the role of other neurotransmitters in the formation and maintenance of delusions. Knowledge of other neurotransmitters relevant to delusions could pave the way for developing more effective pharmacological interventions for managing delusional beliefs. Lastly, it would be useful to extend research in people who are ‘at risk’ of psychosis to explicitly examine brain regions associated with

assessment of certainty (e.g. salience network). This would be clinically useful as metacognitive training programs which specifically target cognitive biases associated with delusions (e.g. JTCs, BADE) show promise in terms of reducing biases, belief-related distress and quality of life for people with delusions (Moritz et al., 2011; Moritz, Veckenstedt, Randjbar, Vitzthum, & Woodward, 2011). Furthermore, cognitive remediation therapy, which teaches cognitive flexibility, working memory and planning skills, may also attenuate high-level cognitive biases and prevent the formation of delusional symptoms (Wykes et al., 2007a; Wykes et al., 2007b). Mindfulness training has also been found to directly regulate function of the salience network (Zeidan et al., 2011), which could provide a low-level intervention for delusions by altering people's objective perception of their environment.

Based on the current paper, future research could test the following specific predictions:

- 1) That high and low-level certainty judgments differ across clinical presentations. Aberrant salience, BADE and JTC might be predicted to be more severe and prominent in schizophrenia than other presentations such as bipolar disorder and psychotic depression. This could be due to the increased delusion severity as well as additional cognitive vulnerabilities associated with a schizophrenia diagnosis (e.g. memory, attention and executive functioning; Bowie & Harvey, 2006) that might further interfere with the capacity to make high and low level certainty judgments.
- 2) That high and low level certainty judgments relate to phenomenological differences in the delusional experience. Specifically, biases such as JTC might be associated with complex or affective delusions and altered dopamine in the absence of higher-level biases may be related to passivity phenomena and delusions of reference.
- 3) That people with delusions who report more extreme emotions and/or past trauma would demonstrate exaggerated alterations in high and low level certainty judgments (i.e. increased alterations to the dopaminergic system, aberrant salience and cognitive biases).
- 4) That specific, monothematic delusions arise from a disrupted dopaminergic system and aberrant salience (i.e. low level certainty) but intact high level certainty judgments. To that end, that correction of high-level cognitive biases would significantly weaken complex delusions, but would have little effect on monothematic delusions or passivity phenomena.

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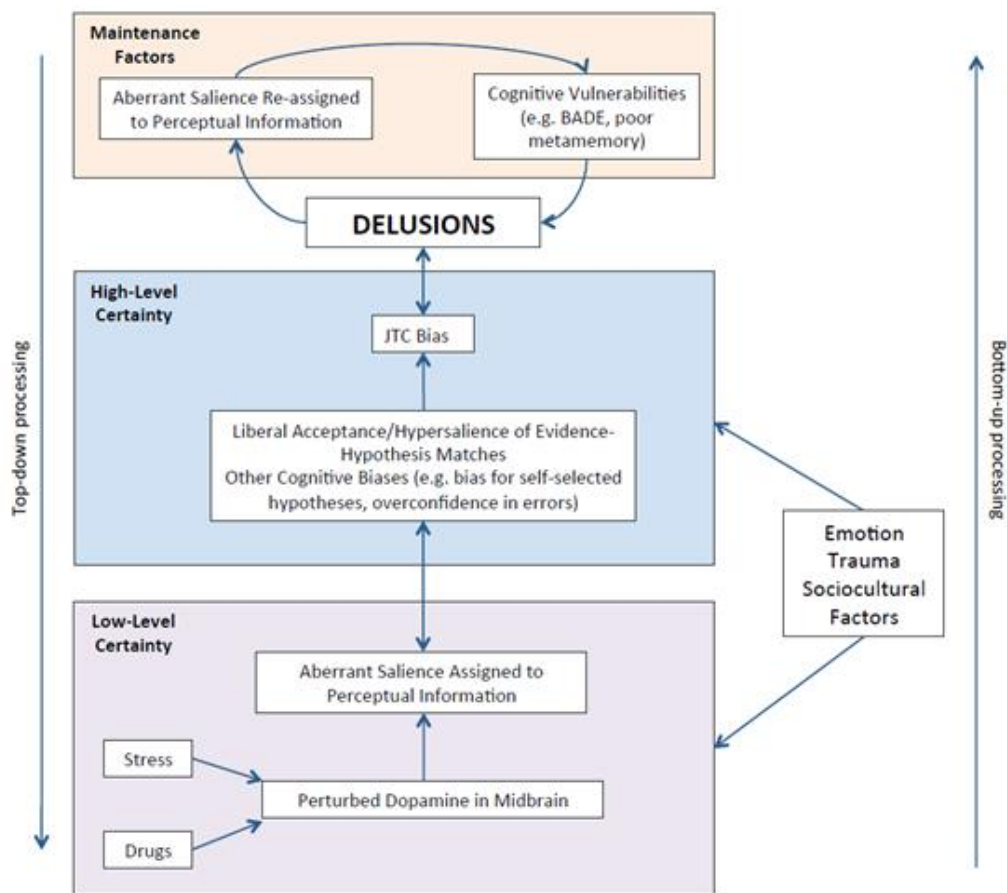


Figure 1

Highlights

- Delusions are conceptualised as arising through alterations in certainty judgments
- Certainty assessments depend on both low and high level neurocognitive processes
- Dopamine, aberrant salience and JTC bias are empirically associated with delusions
- Trauma, emotion and sociocultural factors may interact with these processes
- A neurocognitive model for delusion formation and maintenance is proposed

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